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Hoechst Aktiengesellschaft
Pharma Research
Toxicology

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Mucosal tolerance to

Ma Ref 0380

in the rabbit

Report No. 1092/77

Summary

The results of mucosal tolerance testing under the test conditions described have shown that Ma Ref 0380 can be regarded as being non-irritant to mucous membranes if eyes treated with the preparation are cleansed with water one minute after application. If such cleansing is not carried out, Ma Ref 0380 has a slight irritant effect on mucous membranes.

Ma Ref 0380 = Shampoo with
0.3 % Octopirox

/2

31777-7110

Vorsitzender des Aufsichtsrats: Karl Winnacker · Vorstand: Rolf Sammet, Vorsitzender, Kurt Lanz, stellv. Vorsitzender; Erhard Bouillon, Rudolf Frank, Enrique Hartung, Wolfgang Hilger, Willi Hoerkens, Josef Nowotny, Wolfgang von Polnitz, Hans Reintges, Jürgen Schaahausen, Hans Schlachter, Klaus Wessermel, stellv. Martin Fruhaut · Sitz der Gesellschaft Frankfurt am Main · Handelsregister Frankfurt am Main Abt. B Nr. 14500

Implementation of the Trial

We tested mucosal tolerance to Ma Ref 0380 in six albino Himalayan rabbits by a single application of 0.1 ml of a 1 : 1 dilution of the preparation in water into the conjunctival sac of the rabbits' left eyes. 0.1 ml of water was applied into the conjunctival sac of the right eyes as a control. Both eyes of three of the six treated animals were cleansed one minute after application, using 20 ml of water in each case. Warm tap water (37 °C) with a pH value of 7.3 and a degree of hardness of 21 °dH [deutsche Härtegrad = German degree of hardness] was used for rinsing out the eyes.

The results were assessed with the aid of a magnifying glass 10, 60, 180 and 330 minutes after treatment and also after 24, 48 and 72 hours. The 24, 48 and 72-hour findings were obtained following instillation of one drop of fluorescein sodium in a 1 : 10 000 dilution = 0.01 %. Once these assessments had been completed, the treated eyes were rinsed out with physiological saline solution.

Results:

Under the above-mentioned test conditions, the peak irritant indices of Ma Ref 0380 were found to be:

- 8 in cleansed eyes after 330 minutes;
- 12 in uncleaned eyes after 180 minutes;
- 10 as the mean value in all animals after 180 minutes.

Thus, Ma Ref 0380 can be regarded as being non-irritant to mucous membranes in those animals whose eyes were cleansed one minute after application and as a slightly irritant in all the animals whose eyes were not cleansed.

Dr. Ma/Ju
30th November 1977

Pharma Research
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Dr. Mayer
Head of Laboratory

Dr. Weigand
Coordination
Industrial Toxicology

Scale for Scoring Ocular Lesions

(1) Cornea	
(A) Opacity-degree of density (area most dense taken for reading)	
No Opacity	0
Scattered or diffuse area, details of iris clearly visible	1
Easily discernible translucent areas, details of iris slightly obscured.....	2
Opalescent areas, no details of iris visible, size of pupil barely discernible.....	3
Opaque, iris invisible.....	4
(B) Area of cornea involved	
One quarter (or less) but not zero.....	1
Greater than one quarter, but less than half.....	2
Greater than half, but less than three quarters.....	3
Greater than three quarters, up to whole area.....	4
A X B X 5	Total maximum = 80
(2) Iris	
(A) Values	
Normal.....	0
Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris still reacting to light (sluggish reaction is positive).....	1
No reaction to light, hemorrhage, gross destruction (any or all of these).....	2
A X 5	Total maximum = 10
(3) Conjunctivae	
(A) Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)	
Vessels normal.....	0
Vessels definitely injected above normal.....	1
More diffuse, deeper crimson red, individual vessels not easily discernible....	2
Diffuse beefy red.....	3
(B) Chemosis	
No swelling.....	0
Any swelling above normal (includes nictitating membrane).....	1
Obvious swelling with partial eversion of lids.....	2
Swelling with lids about half closed.....	3
Swelling with lids about half closed to completely closed.....	4
(C) Discharge	
No discharge.....	0
Any amount different from normal (does not include small amounts observed in inner canthus of normal animals).....	1
Discharge with moistening of the lids and hairs just adjacent to lids.....	2
Discharge with moistening of the lids and hairs, and considerable area around around the eye.....	3
Score (A + B + C) X 2	Total maximum = 20

The scores for cornea (1), iris (2), and conjunctiva (3) obtained in each rabbit at the specific reading time are added to give the primary irritation score. The mean of the scores for all rabbits at the specific reading time is calculated. The highest score obtained at any of the reading times is used for the evaluation and the substance is categorized as follows:

0 - 10	Non-irritant	(nicht reizend)
11 - 25	Slightly irritant	(leicht reizend)
26 - 56	Moderately irritant	(mäßig reizend)
57 - 110	Severely irritant	(stark reizend)

Annex

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Schleimhautverträglichkeit / Eye irritation

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Schleimhautverträglichkeit / Eye irritation

EVALUATION OF CORNEA AFTER INSTILLATION OF ONE DROP
FLUORESCEIN SODIUM 0,01 %

Substance:	Concentration:	Dose:	Species:
Ma Ref 0380	diluted with water 1 : 1	0,1 ml	Albino Hima- layan rabbit
Time:	Opaque area of the cornea		
	Rabbit No.:		
	13	14	15
24 hours after appl.	1/3	NAD	1/3
			NAD
48 hours after appl	NAD	NAD	NAD
			*
72 hours after appl.	NAD	NAD	NAD
			*
Remark: *punctiform, pinhead-sized opacity of the cornea			

Substance:	Concentration:	Dose:	Species:
water (control eye)		0,1 ml	Albino Hima- layan rabb
Time:	Opaque area of the cornea		
	Rabbit No.:		
24 hours after appl.			
48 hours after appl.			
72 hours after appl.			
Remark: *punctiform, pinhead-sized opacity of the cornea			